REMARKS

Claims 1-120 and 142-158 have been canceled. Claims 121-141 are pending and are currently under consideration.

A. Interview Summary

Applicants again thank Examiner Rawlings and Supervisory Examiner Helms for the telephone interviews of September 20, 2006, continuing to September 21, 2006, in which the claims, the content of the specification and the rejections of record were discussed as follows:

1. Figures 8 and 9, which illustrate binding of modified antibodies to denatured collagen over native collagen. Applicants also pointed the Examiner to paragraph [0036] of the application which discloses antibodies having a higher binding affinity for denatured collagen versus native collagen. In view of the disclosure of the specification and the data presented in Figures 8 and 9, Examiner Rawlings and Supervisory Patent Examiner Helms acknowledged that the application provides working examples of modified antibodies having higher binding affinity for denatured collagen versus native collagen and agreed that the claims do not have to recite "at least 2-fold" higher binding affinity.

Independent claims 121 and 131 recite an antibody, or antigen-binding fragment thereof, which has higher binding activity for denatured collagen over native collagen. Claim 141 recites the elected species of an antibody, or antigen-binding fragment thereof, which binds to denatured collagen as described in the specification. The antibodies or antigen-binding fragments thereof, recited in the current claims have a function associated with the structure.

2. During the interview, Applicants discussed Figures 4C and 6 of the application with Examiner Rawlings and Supervisory Patent Examiner Helms. Modifications of amino acid residues in one or more heavy and/or light chain CDRs of HUIV26 variants presented in the figures represent modifications made as compared to the wild-type sequence. Furthermore, Applicants faxed the Examiner a series of Tables which illustrated modifications made to heavy and light chain CDRs and which included references to the sequence identifiers containing the modifications. Applicants further provided these Tables with the previous response as Exhibit A for entry into the file. (Request for Continued Examination, filed March 20, 2007, Exhibit A). The application

demonstrates, therefore, possession of a genus of antibodies which are supported by sequences of modified CDRs presented in the Figures, the description and the Sequence Listing. Applicants have shown how to make and use modified antibodies over the full scope of the claims using the methods described in the application. For these reasons, Applicants asserted that the claims are enabled over the full scope of the claims, have written support throughout the application, and that no new matter has been added by amendment in contrast to the Examiner's assertions of record.

In the interview, the Examiner indicated that the modifications (discussed above) presented in the Examiner's proposed amendment were found in Figure 4C of the application. As discussed in the interview, Applicants respectfully submit that the application contains more modifications in the CDRs than found in Figure 4C. Support for other CDR modifications can be found, for example, in Figure 6, in paragraphs [0043], [0049] and [0061] to [0078] of the published application, the originally-filed claims and the Sequence Listing – all of which are indicated in Exhibit A (Request for Continued Examination, filed March 20, 2007, Exhibit A).

3. Applicants thank Examiner Rawlings for acknowledging that the modified HUIV26 antibodies are novel and for agreeing to allow composition claims of antibodies reciting specific combinations of CDRs which were presented in the specification.

4. Applicants thank Examiner Rawlings and Supervisory Patent Examiner Helms for acknowledging that the application provides examples of modified antibodies having conservative and/or non-conservative modifications.

5. In response to the Examiner's previous statements of record, that the structure of variant of DhuG5 of Figure 8 was not presented in the specification, Applicants directed the Examiner to Figure 6 and discussed the Figure with respect to modifications made compared to the wild-type sequence CDRs. Applicants thank Examiner Rawlings and Supervisory Patent Examiner Helms for acknowledging that the structures of all of the variants presented have been disclosed, either in the specification, the Figures, and/or the Sequence Listing showing possession of the claimed compositions.

Thus, no new matter has been recited in the claims presented, or in the claims of record. Furthermore, Applicants have not made any additions to the specification.

6. Applicants submit that the claims have been amended solely to further prosecution; such amendments are not to be taken as acquiescence to the Examiner's rejections. Applicants reserve the right to prosecute any canceled subject matter in continuing and/or divisional applications.

B. Support for the amended claims

Specific non-limiting examples of support for the claims as recited are provided below:

- Specific support for all of the modifications made to the CDRs can be found, for example, in the claims, as originally filed, Figure 4C, Figure 6, the sequence listing, as originally filed, and in paragraphs [0049], [0052] and [0060] to [0078]. As discussed above, Applicants previously provided tables of modifications discussed during the interview in which Applicants pointed out support for modifications represented in the specification, the figures and the sequence listing (summarized in Exhibit A). Each of the amino acid modifications recited in the claims herein can be found in one or more of these locations. (Claims 121 and 131.)
- Support for grafted antibodies can be found, for example, at paragraphs [0095] to [0097] and in Example V of the specification. (Claims 122, and 131 to 140.)
- Support for antigen-binding fragments of antibodies, can be found, for example, at paragraphs [0029] and [0030] of the specification. (Claims 121-141.)
- Support for an antibody, or antigen-binding fragment thereof, having two CDR modifications can be found at, for example, paragraphs [0046], [0050], [0059], and [0061] of the specification. (Claims 124 and 137.)
- Support for an antibody, or antigen-binding fragment thereof, having three CDR modifications can be found at, for example, paragraphs [0062], [0063] and [0078] of the specification. (Claims 125 and 138.)
- Support for an antibody, or antigen-binding fragment thereof, having four CDR modifications can be found at, for example, paragraphs [0065], [0067], [0069] and [0074] of the specification. (Claims 126 and 139.)

- Support for an antibody, or antigen-binding fragment thereof, having five CDR modifications can be found at, for example, paragraphs [0064], [0066], [0068], [0071] to [0073] and [0075] to [0077] of the specification. (Claims 127 and 140.)
- Support for nucleic acids can be found, for example, at paragraphs [0028] and [0153] to [0155] of the specification. (Claims 128 and 134.)
- Support for antibodies further comprising therapeutic or detectable moieties can be found, for example, at paragraph [0170] of the specification. (Claims 129, 130, 135 and 136)

As all of the amendments are supported by the original disclosure, no new matter has been added. The above amendments have been made for reasons unrelated to patentability and should not be construed as constituting any admission with respect to the patentability of the previously claimed subject matter.

Also, in the current office action drafted by the Examiner, Applicants respectfully point out that the Examiner cites claims 89-100 as pending and further states that claims 89-141 are currently under prosecution. However, it is claims 121-158 that were previously presented and under prosecution, thus Applicants are unsure of the basis for the citation to 89-100 and 89-141 as well as the subsequent rejections based on the aforementioned citation of these claims. Despite this apparent discrepancy in subject matter of the rejection and solely in an effort to further prosecution, Applicants have amended the claims as discussed above and submit that these amendments render the Examiner's rejections moot with respect to the currently amended claims, as further discussed below.

C. Rejections under 35 U.S.C. § 112

1. 35 U.S.C. § 112, 2, indefinite claims

The Examiner has rejected claims 124-128 and 137-140 as being indefinite. Applicants maintain for reasons of record that the claims as previously filed particularly and distinctly point out the subject matter that Applicants regard as the invention. However, solely to further prosecution, Applicants have amended the claims as discussed above. Thus, Applicants submit that the rejection under 35 U.S.C. § 112, ¶ 2 is moot based on the current amendments to the claims and respectfully request that the Examiner withdraw the rejection.

2. 35 U.S.C. § 112, 1, scope of enablement

a. As discussed during the interviews, the specification contains a dense amount of information describing how to make and use antibodies having modified sequences. Briefly, the specification fully recites how to make and use the antibodies as currently recited: see, for example, paragraphs [0098] to [0180], Examples III, IV, and VI and Figures 6-11.

With respect to the structure of the recited antibodies, the specification recites a representative number of species of antibodies, or antigen-binding fragments thereof, having CDRs containing conservative modifications, non-conservative modifications, or a combination thereof, that were made using the techniques described in the Detailed Description and Examples.

With respect to the function of the recited antibodies, Figure 6 illustrates that the modified antibodies, and antigen-binding fragments thereof, are able to bind denatured collagen as demonstrated by the association and dissociation rates. Figure 8 illustrates that modified antibodies, and antigen-binding fragments thereof, made using the methods recited in the specification bind with higher affinity to denatured collagen over native collagen.

b. Solely in an effort to further prosecution, Applicants have amended the claims to recite antibodies having at least one modification in at least one CDR wherein the specific substitutions are provided in the application and to remove the recitation of "at least 2-fold" higher binding affinity in view of the discussions above. However, Applicants maintain for the reasons of record that the claims as previously filed are fully enabled.

Based on the disclosure of the specification, including the Examples, Tables, Figures and Sequence Listing, Applicants submit that Examiner Rawlings and Supervisory Examiner Helms agreed during the telephonic interviews of September 20 and 21, 2006, that the claims as recited are fully supported. That is, the specification fully describes how to make and use such antibodies as currently claimed.

Applicants submit that the rejection of the claims under 35 U.S.C. § 112, first paragraph, is moot based on these amendments, and respectfully request that the rejections of claims under 35 U.S.C. § 112, ¶ 1, scope of enablement be withdrawn.

3. 35 U.S.C. § 112, 1 – Written Description

Applicants again respectfully point out that the Examiner has cited claims 89-140 failing to comply with the written description requirement. As noted above, many of these cited claims do not exist in the currently pending application and/or appear to reference claims previously presented and since cancelled or amended. Thus, Applicants are unsure of the basis for the Examiner's current rejection given the citation to claims no longer pending and/or presented. Moreover, Applicants' position regarding the application and support for the claims has been discussed above.

Solely in an effort to further prosecution, Applicants have amended the claims as discussed above. The application clearly demonstrates that Applicants invented and were in possession of what is claimed based on the written description guidelines. Applicants maintain for reasons of record that the claims as previously filed are fully supported by the application.

Applicants submit that the rejection of the claims under 35 U.S.C. § 112, first paragraph, is moot based on these amendments, and respectfully request that the rejections of claims under 35 U.S.C. § 112, ¶ 1, written description be withdrawn.

D. Rejections under 35 U.S.C. § 102 and/or 103

The Examiner has stated that the claims do not distinguish the present invention materially, structurally, or functionally from the antibodies described by *Hybridoma*. 2000 Oct; 19(5):375-85) (Xu et al., of record) and WO 00/40596 A1 (Brooks et al.) and are thus anticipated by either reference under 102(b) or by Brooks et al. under 103(a).

In light of the amendments to the claims presented herein and discussed above, Applicants submit that the amended claims are not anticipated nor made obvious by Xu et al. or Brooks et al.. The claims now distinctly recite an antibody that is a variant of the HUIV26, that binds denatured collagen type IV, and that further contains one or more CDRs that differ from the corresponding CDRs of HUIV26. Further, the substitutions available within the CDRs are also identified in the amended claims and supported by the specification as discussed above. The antibodies having specific substitutions are not disclosed by Xu et al. or Brooks et al., and Applicants further submit that such antibodies and/or substitutions are not obvious in light of Brooks et al. Thus, Applicants

submit that the amendments render the rejections moot and respectfully request that the Examiner withdraw the rejections under 102(b) and 103(a).

CONCLUSION

Applicants believe that for the reasons set forth above, the Examiner's rejection of the claims have been overcome. Thus, Applicants respectfully request that the Examiner allow the composition claims and rejoin the method claims.

This amendment is filed on December 5, 2007. Applicants believe this amendment is timely filed within six (6) months of the mailing date of the action and submit a petition for a 3-month extension of time and associated fee herewith. However, if the Office determines that any additional fee is due, please charge Deposit Account No. 23-2415 (referencing docket no. 30795-711.201).

If the Office believes, for any reason, that personal communication will expedite prosecution of this application, the Office is invited to telephone the undersigned at (858) 350-2300.

Respectfully submitted,

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